Complete Summary

GUIDELINE TITLE

Management of non-muscle-invasive bladder cancer.

BIBLIOGRAPHIC SOURCE(S)

American Urological Association, Inc. Report on the management of non-muscle-invasive bladder cancer. Baltimore (MD): American Urological Association, Inc.; 1999. 66 p. [108 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Non-muscle-invasive bladder cancer (stages Ta, T1 and Tis)

GUIDELINE CATEGORY

Management
Treatment

CLINICAL SPECIALTY

Internal Medicine
Oncology
Urology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To analyze the literature regarding available methods of treating non-muscle-invasive bladder cancer.
- To make practice policy recommendations based primarily on treatment outcomes data.

TARGET POPULATION

The Panel defined 3 specific types of patients (index patients) to whom recommendations apply:

- Index patient 1 presents with an abnormal growth on the urothelium but has not yet been diagnosed with bladder cancer
- Index patient 2 has established bladder cancer of any grade, stage Ta or T1, with or without carcinoma in situ but has not had prior intravesical therapy
- Index patient 3 has carcinoma in situ or high grade T1 cancer and has had at least one course of intravesical therapy

INTERVENTIONS AND PRACTICES CONSIDERED

1. Transurethral resection of a bladder tumor (TURBT)
2. TURBT plus thiotepa
3. TURBT plus doxorubicin
4. TURBT plus mitomycin C
5. TURBT plus bacillus Calmette-Guerin (BCG)

MAJOR OUTCOMES CONSIDERED

- Probability of tumor recurrence
- Risk of tumor progression
- Complications of treatment

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The guideline developer performed literature searches using the MEDLINE database, restricting retrieval to English language articles on human subjects covering the period from January 1964 to January 1998. Some articles (including some that predate the inception of MEDLINE in 1966) were added for review based on panel members' own knowledge.

The initial MEDLINE search was performed in 1989. A subsequent literature search was performed in 1992 with the search terms bladder neoplasms and carcinoma, transitional cell. Several update searches were also performed, the last in 1998. Update searches were further restricted to articles containing the term superficial in the bibliographic record.

The panel as a group reviewed the abstracts and selected the relevant articles for data extraction. Articles were rejected because of inadequate methods, irrelevant data and duplication of data in a later article from the same source.

NUMBER OF SOURCE DOCUMENTS

The searches identified 5,712 articles, from which the panel ultimately selected 181 for data extraction.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Not stated

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not stated

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis of Observational Trials
Meta-Analysis of Randomized Controlled Trials
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The panel used the confidence profile method to combine data extracted from the 181 articles using meta-analysis computer software. This method produces probability distributions which can be described using a mean or median estimate of the probability and a confidence interval (CI), which is such that the probability (Bayesian) of the true value being outside the interval is 5%. The width of the confidence interval indicates the degree of uncertainty about the estimated probability, reflecting factors such as the differences in outcomes data combined from different studies and the size of the studies. The confidence profile method allows analysis of data from randomized controlled trials and single arm studies that are not controlled. For nonmuscle invasive bladder tumors data from more than 30 randomized controlled trials were available to generate comparative estimates of recurrence and progression probabilities for treatment alternatives (tabulated in the guideline document). However, many of these studies were small and, thus, suboptimal for estimating probabilities of treatment complications, particularly uncommon complications. Therefore, the panel included data from clinical series as well as randomized controlled trials for generating complication estimates (tabulated in the guideline document).

There were 2 approaches used for meta-analysis. For estimates of recurrence and progression, data from multiarmed randomized controlled trials were combined meta-analytically to determine the difference in probability between 2 treatment alternatives (tabulated in the guideline document). All alternatives were compared in pairs. For estimates of treatment complications meta-analysis was performed to combine data from single arms of more than one study, including the relevant single arms of multiarmed randomized controlled trials. An estimate of the

probability of each complication was computed (tabulated in the guideline document).

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Balance Sheets
Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

To develop the recommendations, the American Urological Association (AUA) Bladder Cancer Clinical Guidelines Panel used an explicit approach. This approach attempts to arrive at practice policy recommendations through mechanisms that systematically take into account relevant factors for making selections between alternative interventions. Such factors include estimation of the outcomes from the interventions, consideration of patient preferences and assessment of the relative priority of the interventions for a share of limited health care resources when possible. For estimating the outcomes of interventions, emphasis is placed on the use of scientific evidence. When panel opinion is necessary, the explicit approach calls for explaining why it was necessary and/or for discussion of the factors considered.

In developing its recommendations, the panel made an extensive effort to review the literature on non-muscle-invasive bladder cancer and to estimate outcomes of alternative treatment modalities as accurately as possible. The panel members themselves served as proxies for patients in considering preferences with regard to health and economic outcomes.

The panel generated its recommendations based on the probability estimates shown in the outcomes tables and on expert opinion. These recommendations were graded according to three levels of flexibility as determined by strength of evidence and the expected amount of variation in patient preferences. The three levels of flexibility are standard, guideline, and option. See the "Rating Scheme for the Strength of the Recommendations" field.

A standard has the least flexibility. A guideline has significantly more flexibility, and options are the most flexible. In this report, the terms are used to indicate the strength of the recommendations. A recommendation was labeled a standard, for example, if the panel concluded that it should be followed by virtually all health care providers for virtually all patients. A guideline generally denotes a recommendation supported by objective data but not with sufficient strength to warrant a designation of standard. An option in this report would include treatments for which there appears to be equal support in the literature or ones for which there is insufficient published information to support a stronger recommendation. Also, as noted in the "Rating Scheme for the Strength of the Recommendations" field, options can exist because of insufficient evidence or because patient preferences are divided. In the latter case particularly, the panel considered it important to take into account likely preferences of individual patients with regard to health outcomes when selecting from among alternative interventions.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

The panel graded practice policy recommendations according to the levels of flexibility determined by the strength of evidence and the expected amount of variation in patient preferences. The three levels of flexibility are defined as follows:

Standard: A treatment policy is considered a standard if the health and economic outcomes of the alternative interventions are sufficiently well-known to permit meaningful decisions and there is virtual unanimity about which intervention is preferred.

Guideline: A policy is considered a guideline if (1) the health and economic outcomes of the interventions are sufficiently well-known to permit meaningful decisions and (2) an appreciable but not unanimous majority agree on which intervention is preferred.

Option: A policy is considered an option if (1) the health and economic outcomes of the interventions are not sufficiently well-known to permit meaningful decisions, (2) preferences among the outcomes are not known, (3) patients' preferences are divided among the alternative interventions and/or (4) patients are indifferent about the alternative interventions.

COST ANALYSIS

A formal cost analysis was not performed and published cost-analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The panel graded practice policy recommendations according to the levels of flexibility determined by the strength of evidence and the expected amount of variation in patient preferences. The three levels of flexibility are defined as follows:

- Standard: A treatment policy is considered a standard if the health and economic outcomes of the alternative interventions are sufficiently well-known to permit meaningful decisions and there is virtual unanimity about which intervention is preferred.

- Guideline: A policy is considered a guideline if (1) the health and economic outcomes of the interventions are sufficiently well-known to permit meaningful decisions and (2) an appreciable but not unanimous majority agree on which intervention is preferred.
- Option: A policy is considered an option if (1) the health and economic outcomes of the interventions are not sufficiently well-known to permit meaningful decisions, (2) preferences among the outcomes are not known, (3) patients' preferences are divided among the alternative interventions and/or (4) patients are indifferent about the alternative interventions.

Recommendations for all index patients

Standard:

Physicians should discuss with the patient the treatment options and the benefits and harms, including side effects, of intravesical treatment, especially those side effects associated with a particular agent.

Recommendation for Index Patient No. 1

A patient who presents with an abnormal growth on the urothelium but who has not yet been diagnosed with bladder cancer:

Standard:

If the patient does not have an established histologic diagnosis, a biopsy should be obtained for pathologic analysis.

Recommendations for Index Patient No. 2

A patient with established bladder cancer of any grade, stage Ta or T1, with or without carcinoma in situ (CIS) but has not had prior intravesical therapy

Standard:

Complete eradication of al visible tumors should be performed if surgically feasible and if the patient's medical condition permits.

Option:

Surgical eradication can be performed by one of several methods, including electrocautery resection, fulguration or laser ablation.

Option:

Adjuvant intravesical chemotherapy or immunotherapy is an option for treatment after endoscopic removal of low-grade Ta bladder cancers.

Guideline:

Intravesical instillation of either BCG or mitomycin C is recommended for treatment of CIS and for treatment after endoscopic removal of T1 tumors and high-grade Ta tumors.

Option:

Cystectomy may be considered for initial therapy in some patients with CIS or T1 tumors.

Recommendations for Index Patient No. 3

A patient with CIS or high grade T1 cancer and has had at least one course of intravesical therapy

Option:

Cystectomy may be considered as an option for patients with CIS or high-grade T1 cancers that have persisted or recurred after an initial intravesical treatment.

Option:

Further intravesical therapy may be considered as an option for patients with CIS or high-grade T1 cancers that have persisted or recurred after an initial intravesical treatment.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The panel based treatment recommendations on analysis of comparative outcomes data from randomized controlled trials and on expert opinion.

The panel followed an explicit approach to the development of practice policy recommendations. This approach emphasizes the use of scientific evidence in estimating outcomes. If the evidence has limitations, the limitations are clearly stated. When panel opinion is necessary, the explicit approach calls for an explanation of why it is necessary and/or for a discussion of the factors considered.

Recommendation for all index patients: This recommendation is based on the panel's expert opinion.

Recommendations for Index Patient No. 2: The first recommendation (Standard) and the second recommendation (Option) are based on the panel's expert opinion. The third recommendation (Option) is based on the evidence in the outcomes tables. The fourth recommendation (Guideline) is based on evidence from the

literature and panel opinion. The fifth recommendation (Option) is based on the panel's expert opinion.

Recommendations for Index Patient No. 3: The first recommendation (Option) is based on panel opinion rather than evidence in the outcomes tables. The second recommendation (Option) is based on the panel's expert opinion.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

All of the intravesical agents (thiotepa, bacillus Calmette-Guerin, mitomycin C and doxorubicin) when used as adjuvant therapy after transurethral resection resulted in a lower probability of recurrence compared to resection alone. However, there is no evidence that intravesical therapy affects long-term progression. Refer to the guideline document for the calculated estimates of the probability of recurrence and progression for each intravesical agent compared to resection alone and to each of the other agents.

POTENTIAL HARMS

Adverse outcomes are grouped into local bladder symptoms, systemic symptoms and other. Local bladder symptoms were the most common adverse outcomes for patients undergoing treatment for nonmuscle invasive bladder cancer. The most frequently observed immediate symptoms were irritative lower urinary tract problems, including dysuria, frequency/nocturia, urgency, pain and cramping, and passing of debris in the urine, including blood or clots. Patients also experienced bacterial cystitis, urinary incontinence and bladder perforation. Long-term adverse outcomes related to local bladder symptoms included bladder contracture. Although local bladder symptoms can be severe, systemic symptoms were more threatening and included flush-like symptoms, such as arthralgia, fever, chills and malaise. Systemic infectious complications also resulted from treatment, including pulmonary or hepatic changes, pneumonia, pneumonitis, hepatitis, epididymitis, prostatitis and urethral infection. Some patients had nausea, vomiting, rash or indirect adverse outcomes, such as myelosuppression.

Refer to the original guideline document for specific estimates of the probability of each complication associated with each intervention.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

American Urological Association, Inc. Report on the management of non-muscle-invasive bladder cancer. Baltimore (MD): American Urological Association, Inc.; 1999. 66 p. [108 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1999

GUIDELINE DEVELOPER(S)

American Urological Association, Inc. - Medical Specialty Society

SOURCE(S) OF FUNDING

The American Urological Association (AUA) is the sole source of funding.

GUIDELINE COMMITTEE

Bladder Cancer Guidelines Panel

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Members: Joseph A. Smith, Jr., MD (Chair); Richard F. Labasky, MD (Facilitator); James E. Montie, MD; Randall G. Rowland, MD; Abraham T.K. Cockett, MD; John A. Fracchia, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

An update is not in progress at this time.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the American Urological Association Web site.

Print copies: Available to physicians from the American Urological Association, Inc., 1000 Corporate Boulevard, Linthicum, MD 21090; telephone: (866) RING AUA.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

The following is available for physicians to distribute to patients:

- Smith JA Jr, Labasky RF, Montie JE, Rowland RG, Cockett AT, Fracchia JA. Doctor's guide for patients on management bladder cancer. Baltimore, MD: American Urological Association, 1999. 10 p.

For print copies, physicians may contact: American Urological Association, Inc., 1000 Corporate Boulevard, Linthicum, MD 21090; Website: www.auanet.org; telephone (410) 223-4367.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This summary was completed by ECRI on January 5, 2000. It was verified by the guideline developer on January 14, 2000.

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